

Six-year outcomes of carotid artery stenting performed with multidisciplinary management in a single center

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ABSTRACT

Objective: This study aimed to evaluate the first 30-day results of clinical, periprocedural asymptomatic cranial embolism, and long-term restenosis of the multidisciplinary conducted and evaluated carotid artery stenting (CAS) procedure in our patient group with real-life data.

Methods: A total of 610 patients who were subjected to consecutive CAS procedures in our center between December 2010 and February 2019 were clinically and radiologically followed up for a mean duration of 6 years. Of the 610 patients, 274 (45%) were symptomatic for carotid artery stenosis, whereas 336 (55%) were identified as asymptomatic. As embolism protection methods, distal protection, proximal protection, and double (distal + proximal) protection was used in 52%, 43%, and 0.3% of patients, respectively.

Results: The success rate of the CAS procedure was 96%. Procedure-related death was reported in 4 (0.6%) patients who successfully underwent the CAS procedure. Moreover, acute carotid artery stent thrombosis, hyperperfusion syndrome, periprocedural major stroke, and periprocedural minor stroke was observed in 4 (0.6%), 2 (0.3%), 2 (0.3%), and 12 (1.9%) patients, respectively. The total clinical complication rates during the first 30 periprocedural days were 1.6% (10 patients) and 3.1% (19 patients) in the asymptomatic and symptomatic groups, respectively. On cranial magnetic resonance imaging performed, asymptomatic ipsilateral cranial microembolism, asymptomatic contralateral cranial microembolism, and bilateral asymptomatic cranial microembolism was detected in 61 (11.6%), 20 (3.8%), 23 (4.4%) patients, respectively. Asymptomatic restenosis was observed in 24 (3.9%) patients.

Conclusion: The CAS procedure is a reliable treatment option applicable with acceptable complication and success rates as outlined in the guidelines, when performed following a multidisciplinary evaluation, in the treatment of symptomatic and asymptomatic carotid artery stenosis, including high-risk patient groups.

Key words: carotid artery stenting, Multidisciplinary Carotid Committee, stent restenosis, stroke

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Introduction

Atherosclerosis is responsible for one-third of all strokes and 90% of cerebral thromboembolic events. The treatment of symptomatic or asymptomatic severe carotid artery atherosclerotic stenosis is carotid artery stenting (CAS) and is currently recommended as an alternative to carotid artery endarterectomy (CEA) in high-volume and experienced centers (1, 2). Literatures clearly demonstrate that the success of CAS depends on specialist experience (3). Among CAS studies performed to date, the long-term results of CAS procedures jointly

performed by a neurologist and cardiologist in a high-volume single center, following a multidisciplinary evaluation have not been published. In this study, we aimed to evaluate the mean 6-year outcomes of the CAS procedure, which was decided, implemented, and followed up using a multidisciplinary approach, and share experiences as regards the management of specific patient groups. The primary outcome of our study was clinical complications within the first 30 days after CAS, whereas the secondary outcomes were periprocedural asymptomatic cranial embolisms and carotid stent restenosis after 30 days.

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HIGHLIGHTS

- The most important early complication of carotid artery stenting (CAS) procedure is new ischemic brain lesions due to distal embolization. The most important long-term complication of the CAS procedure is stent restenosis.
- CAS procedure, which is performed with a multidisciplinary evaluation, can be performed with high success and low complication rates even in risky patient groups.

Methods

Retrospectively, data of 610 consecutive (mean age, 71.3 years) patients who were admitted at our center from December 2010 to February 2019 were evaluated and discussed at our Multidisciplinary Carotid Committee, which consisted of neurology, cardiology, cardiovascular surgery and radiology clinics. Symptomatic patient was defined as having a history of ischemic cerebrovascular disease with or without any sequelae, transient ischemic attack (TIA), and amaurosis fugax within the last 6 months. The evaluation included patients who were symptomatic with >50% stenosis in digital subtraction angiography (DSA) according to the NASCET formula and those who were asymptomatic with >80% stenosis.

Owing to the large number of patients evaluated in the study, percentage figures were rounded off to the nearest decimal value.

Patient selection—functions of the Multidisciplinary Carotid Committee

All patients were first evaluated by a neurologist specialized in stroke and discussed at the carotid committee after necessary clinical consultations were performed. At the committee, the neurologist presented cranial imaging and clinical findings on whether the patient was symptomatic or asymptomatic. A total of 1427 patients were evaluated in the committee. It was decided to perform CEA surgery in 410 patients and CAS in 670 patients. The first 31 patients who underwent CAS in our center were excluded from the analysis because they were within the learning curve period, a multidisciplinary carotid council had not

yet been formed, and cranial diffusion magnetic resonance (CDMR) was not performed. A total of 635 patients who were decided to undergo CAS by the Multidisciplinary Carotid Committee were taken to the catheter laboratory. CAS was not performed in 25 patients, including 11 whose aortic arch anatomies were not suitable, 12 whose carotid arteries were severely tortuous, and 2 whose iliac arteries were occluded. A total of 610 patients were included in the final analysis. CAS was successfully performed at the right brachial artery in one patient who initially could not undergo CAS due to iliac artery stenosis. The other 24 patients were referred for CEA surgery. The Multidisciplinary Committee reviewed in detail the aortic arch anatomy and carotid tortuosity of the last 200 patients. Patients with difficult or risky vascular anatomy (tortuous carotid artery, type 3 aortic arch) for the CAS procedure were referred for CEA surgery.

All patients with a glomerular filtration rate (GFR) above 60 mL/min/1.73 m² were subjected to computed tomography angiography (CTA) of the carotid arteries (Fig. 1a, 1b) after carotid Doppler ultrasonography (USG). The patient's carotid Doppler USG and carotid artery CTA were interpreted together with the radiologist. Upon multidisciplinary medical follow-up, a CAS or CEA decision was made based on the clinical characteristics, concomitant diseases, and carotid artery lesion characteristics of the patient. The CAS or CEA decision was based on the following basic criteria. These criteria were the result of the experience of our center. The committee tended to make a CEA decision as follows: there is a presence of femoral or brachial access problem, the aortic arch in the CTA was highly atherosclerotic or calcific, the carotid artery lesion length was >40 mm, the common carotid artery was highly tortuous, the diameter of the 2-cm parts of the internal carotid artery (ICA) close to the carotid bifurcation and the common carotid arteries was >10 mm, the carotid artery CTA showed a circular calcification surrounding the entire artery in the stenosis region (carotid stent apposition is insufficient and the rate of restenosis is high), there was severe ulceration, a thrombus was observed in the carotid plaque (CAS becomes risky in terms of embolic complications), laboratory tests showed a GFR below 30 mL/min/1.73 m², and a resistance to both acetylsalicylic acid and clopidogrel was detected (Table 1). In other cases, the intervention to the carotid artery was performed by stenting.



Figure 1. (a) Computed tomography angiography image of the left internal carotid artery (b) Three-dimensional computed tomography angiography image of the left internal carotid artery (c) Three-dimensional computed tomography angiography image of the 100% occluded stent in the left internal carotid artery

Table 1. Patient groups considered at risk for carotid artery stenting and referred for carotid endarterectomy surgery

Patient or lesion characteristic
Femoral or brachial access problem
Highly atherosclerotic or calcified aortic arch
Highly tortuous common carotid artery
Carotid artery lesion length >40 mm
Carotid artery diameter close to bifurcation >10 mm
Circular calcification in the carotid artery in the stenosis region
Carotid artery plaque seriously ulcerated or thrombosed
GFR <30 mL/min/1.73 m ²
Resistance to acetylsalicylic acid and clopidogrel

GFR - glomerular filtration rate



Figure 2. Digital subtraction angiography image of symptomatic 99% carotid artery stenosis planned for carotid stent procedure with proximal protection

Preparing patients for carotid artery stenting

Patients referred to CAS by the Multidisciplinary Committee were invited to our center with their relatives. The necessity of performing CAS, technique and complications of the procedure

as well as the early and late postprocedural follow-ups were explained to the patients in detail. Antihypertensive, antihyperlipidemic, and antiplatelet drugs were regulated. The procedure was performed after the blood pressure was regulated below 135/80 mm Hg. It was ensured that patients had been receiving dual antiplatelet treatments composed of 100 mg of acetylsalicylic acid and 75 mg of clopidogrel for at least 7 days. Otherwise, additional loading and maintenance antiplatelet treatments were planned. On the morning of the procedure, venous blood resistance tests were performed for both antiplatelet agents. We used the PFA-100 test to evaluate platelet aggregation in our patients. Off label, if there was only resistance to clopidogrel, CAS was performed with a 90-mg loading dose of two tablets and a two-by-one maintenance dose of ticagrelor. However, if there was resistance to both antiplatelet agents, CAS was not performed, and CEA was recommended for these patients.

Carotid artery stenting

All procedures were performed by two specialists, one invasive cardiologist and the other an interventional vascular neurologist. Prior to the procedure, consent was obtained from all patients. The procedures were performed under local anesthesia via the percutaneous transfemoral route. Throughout the procedure, oxygen saturation, electrocardiography, and blood pressure of patients were monitored. The procedure was initiated using a femoral 8-French (F) sheath. If proximal protection was preferred as the embolism protection method, a 9-F sheath was used. After inserting the sheath, all patients received 75 IU/kg of unfractionated heparin. The 5-F hydrophilic headhunter or sim 1–2 diagnostic catheters were preferred according to the type of aortic arch in the patient's CTA as evaluated by the committee. Following bilateral carotid artery and cerebral DSAs, it was decided as to which emboli protection method will be used, balloon, stent diameters, and whether to perform pre- or postdilatation. It was rather aimed to perform predilatation with a 4.0-by-20 mm or 4.5-by-20 mm balloon before stenting and not to perform postdilatation if the residual stenosis was <30% after stenting. All patients had tapered stents. Self-expandable stent diameter was planned to be 20% larger than the digitally measured diameter of the carotid artery. If the carotid plaque was hard with calcification, mostly a closed-cell stent (Xact Carotid Stent) was preferred, whereas an open-cell stent (sinus-carotid-conical RX stent, RX Acculink, Protege® RX) or a hybrid stent (Cristallo Ideale SE Stent) was preferred for soft plaques. A proximal blocking system (Mo.MA®) was preferred as the embolism protection method (EPM), if the carotid artery stenosis was symptomatic and >90% (Fig. 2), if the contralateral carotid artery was not totally occluded, if the collateral circulation evaluated in the cerebral DSA on the side of the planned carotid artery was not weak, if the ICA was tortuous after bulbous, if the lesion was ulcerated, and if the carotid artery was thrombosed. The distal protection method [Filter (Emboshield, Filterwire, Spider FX)] was applied in other lesions (Fig. 1a, 1b). A prophylactic intravenous dose of 1 mg atropine was administered in patients with heart rates of <60 beats/min before CAS and in those with

heart rates of >60 beats/min, if the heart rate fell below 60 beats/min after carotid ballooning or stenting. In some patients, hypotension did not immediately improve after CAS with atropine. In these patients, normotensive values were achieved with intravenous rapid infusion of saline and norepinephrine. Bilateral cerebral DSA images were taken and compared with pre-CAS images to ensure whether there was post-CAS distal embolization due to the procedure. All patients who did not previously have coronary artery angiography (CAG) had CAG after CAS. The lesions in the CAG were evaluated by the committee, and coronary interventions were planned.

Post-carotid artery stenting follow-up

Clinical and hemodynamic follow-ups after the CAS procedure were performed in all patients for 24 h in the coronary intensive care unit. Intravenous physiological saline solution and norepinephrine infusions were continued for hypotensive patients. In several patients, systemic blood pressures after the procedure were lower than the systemic blood pressures before the procedure owing to the carotid artery stent compression on the carotid sinus. The number of antihypertensive drugs used by patients was reduced. Unlike other centers, CDMR imaging was performed 12–24 h after the CAS procedure to observe possible asymptomatic cranial microembolism. Post-CAS CDMR imaging was performed in 525 (86%) patients. Routine cardiac enzyme follow-up was not performed. Patients were followed up for 24 h after the procedure by a vascular neurologist for minor or major neurological complications. The first month control examination visits for the patients were scheduled before discharge. All patients were prescribed dual antiplatelet and statin (if low density lipoprotein value was >70 mg/dL) during discharge. If the patients had no other specific conditions, the dual antiplatelet treatment was continued for 6–12 months. During the follow-up, maximum efforts were made to ensure that patients received the best medical care. Patients with type 2 diabetes mellitus were followed up at the endocrinology clinic. Patients were followed up and treated in line with the recommendations of the guidelines for heart failure and coronary artery disease. All patients were clinically followed at 1, 3, 6, and 12 months and annually thereafter. Furthermore, stent openness was checked with carotid Doppler USG at 1, 6, and 12 months and annually thereafter. The follow-up period had an average of 36 months and a minimum of 12 months. Carotid CTA was performed in patients with suspected restenosis. An in-stent peak flow rate of ≥ 224 cm/sec in Doppler USG and a $\geq 50\%$ stenosis in CTA were considered as restenosis. Patients who were not followed up with Doppler USG for a minimum of 12 months were not included in the evaluation. The mean incidence of restenosis in patients with restenosis was 9.3 months. In the follow-up Doppler USG of the patients with 100% asymptomatic in-stent occlusion, one of the patients was found to have a total stent occlusion by the sixth month, while two patients reported total occlusion by the 12th month (Fig. 1c). Patients with restenosis were reevaluated by the carotid committee. Restenosis that were asymptomatic and with an intra-stent restenosis rate of $\leq 80\%$ were medically

followed up, while those that were asymptomatic, but with an intra-stent restenosis rate of $\geq 80\%$ were referred for CEA.

Statistical analysis

All statistical analyses were performed using the SPSS 22.0 (Armonk, NY, USA: IBM Corp.). Data were expressed as mean \pm standard deviation for distributed data and percentage for categorical variables.

Results

Patient, lesion, and procedure characteristics

Of the 610 patients who underwent the CAS procedure, 79% were male, 71% were hypertensive, 41% were diabetic, 72% had hyperlipidemia, 75% had coronary artery disease, 2.7% had chronic kidney failure, and 33% were smokers. A total of 45% and 55% of our patients were symptomatic and asymptomatic, respectively. Moreover, 4.9% of symptomatic patients had TIA, 39% had ischemic stroke with sequelae, and 1% had amaurosis fugax. With respect to lesion characteristics, 36%, 33%, and 10% of patients had right ICA stenosis, left ICA stenosis, and bilateral ICA stenosis, respectively, whereas 21% had total occlusion of the contralateral carotid artery. In terms of lesion nature, 36%, 15%, 42%, and 7% of the patients had soft plaque, non-circular calcified plaque, mixed type plaque, and ulcerated plaque, respectively. With respect to the EPM, filtration was preferred in 52%, Mo.Ma[®] in 43%, and double protection (filter + Mo.Ma[®]) in 0.3% of the procedures. CAS was performed without protection in 5% of patients. Open-cell, closed-cell, and hybrid stents were used in 53%, 23%, and 21% of patients, respectively. While 53% of patients were treated only with predilatation, 14% with only postdilatation, and 21% with pre- + postdilatation, 12% had no balloon procedure. Debris was observed in the filter or Mo.Ma[®] aspiration blood in 19% of patients after CAS (Table 2).

Complications

In terms of periprocedural clinical complications in the first 30 days, periprocedural ipsilateral major stroke was observed at a rate of one (0.2%) both in symptomatic and asymptomatic patients in terms of carotid artery lesions. Periprocedural ipsilateral minor stroke was observed at a rate of five (0.8%) in asymptomatic patients and seven (1.1%) in symptomatic patients. Acute carotid artery stent thrombosis was detected in one (0.2%) patient in the asymptomatic group and 3 (0.5%) in the symptomatic group. Hyperperfusion syndrome was not observed in the asymptomatic group, although was observed in 2 (0.3%) in the symptomatic group. Gastrointestinal bleeding was observed in one (0.2%) of the asymptomatic patients, whereas persistent bradycardia was observed in one (0.2%) patient. Acute atrial fibrillation associated with the CAS procedure was observed in 3 (0.5%) of the symptomatic patients. None of the patients experienced myocardial infarction accompanied by electrocardiographic changes. One (0.2%) patient in the asymptomatic group and 3 (0.5%) in the symptomatic group died within the first 30 days of the periprocedural CAS procedure (Table 3).

Table 2. Baseline characteristics of patients and carotid artery stent procedure

Characteristic	n (%)
Age (year)	71.3±9.7
Male	482 (79)
Hypertension	433 (71)
Diabetes mellitus	250 (41)
Hyperlipidemia	439 (72)
Coronary artery disease	458 (75)
Chronic kidney failure	13 (2.7)
Smoking	201 (33)
Symptomatic	274 (45)
Transient ischemic attack	30 (4.9)
Ischemic stroke with sequelae	238 (39)
Amaurosis fugax	6 (1)
Asymptomatic	336 (55)
Internal carotid artery stenosis	
Right ICA	220 (36)
Left ICA	201 (33)
Contralateral carotid with total occlusion	128 (21)
Bilateral ICA stenosis (70%–99%)	61 (10)
ICA lesion characteristics	
Soft	220 (36)
Non-circular calcified	92 (15)
Mixed (soft + punctually calcified)	256 (42)
Ulcerated	43 (7)
Embolism protection method	580 (95)
Distal protection	315 (52)
Proximal protection	262 (43)
Double (Proximal + distal) protection	2 (0.3)
Without protection	31 (5)
Debris +	116 (19)
Stent type	
Open-cell	326 (53)
Closed-cell	142 (23)
Hybrid cell	128 (21)
Balloon	
Predilation alone	323 (53)
Postdilation alone	85 (14)
Pre + post dilation	128 (21)
Without balloon	73 (12)

ICA - internal carotid artery

In terms of periprocedural cardiovascular magnetic resonance (CMR) findings in the asymptomatic and symptomatic groups, the following observations were made: asymptomatic



Figure 3. (a) Digital subtraction angiography image of the right internal carotid artery dissected lesion of a patient who underwent carotid endarterectomy with a hybrid procedure plan. (b) Digital subtraction angiography image of the left internal carotid artery lesion of the patient who underwent carotid stenting with a hybrid procedure plan

ipsilateral microembolism in 30 (5.7%) and 31 (5.9%) patients, asymptomatic contralateral microembolism in 12 (2.3%) and 8 (1.5%) patients, and asymptomatic bilateral microembolism in 9 (1.7%) and 14 (2.7%) patients, respectively. Asymptomatic restenosis was observed in 14 (2.3%) patients in the asymptomatic group and in 10 (1.6%) in the symptomatic group, whereas no symptomatic restenosis was observed in any of the patients. Asymptomatic total occlusion of the stent was observed in two (0.3%) patients of the asymptomatic group and in one (0.2%) in the symptomatic group (Table 4).

Specific patient groups

Six (1%) patients had a longitudinal history of radiotherapy due to laryngeal cancer. Since CEA surgeries are risky in these patients, CAS was suggested by the Multidisciplinary Carotid Committee. Patients with a history of radiotherapy had longer and more complex carotid lesions than those without a history of radiotherapy. By using longer stents, CAS procedures of these patients were also successfully performed.

Secondary CAS procedures were successfully performed in 13 (2.1%) patients with a history of CEA surgery and severe restenosis in the operative area. In these patients, predilation was performed with higher pressure as in patients with a history of radiotherapy.

Thirty-six (6%) patients had hybrid carotid revascularization (Fig. 3a, 3b). With regard to patients who were referred to undergo CAS for the ICA on one side and CEA for the other carotid artery, they first underwent CAS and successfully had CEA 1 month later.

Cranial thrombectomy for tandem occlusion primarily and balloon to the ICA were performed in 13 (2%) patients with a clinical picture of acute ischemic stroke. Four weeks later, the stenting was successfully performed for the residual stenosis in the internal carotid arteries of the patients.

Table 3. Periprocedural 30-day clinical complications

Complication	Asymptomatic Group n (%)	Symptomatic Group n (%)	Total n (%)
Periprocedural ipsilateral major stroke	1 (0.2)	1 (0.2)	2 (0.3)
Periprocedural ipsilateral minor stroke	5 (0.8)	7 (1.1)	12 (1.9)
Acute thrombosis	1 (0.2)	3 (0.5)	4 (0.7)
Hyperperfusion syndrome	0	2 (0.3)	2 (0.3)
Gastrointestinal bleeding	1 (0.2)	0	1 (0.2)
Permanent bradycardia	1 (0.2)	0	1 (0.2)
Acute atrial fibrillation	0	3 (0.5)	3 (0.5)
Myocardial infarction with electrocardiographic change	0	0	0
Death	1 (0.2)	3 (0.5)	4 (0.7)
Total	10 (1.6)	19 (3.1)	29 (4.7)

Table 4. Asymptomatic periprocedural CMR findings and restenosis results after 30 days

Complication	Asymptomatic Group n (%)	Symptomatic Group n (%)	Total n (%)
Asymptomatic ipsilateral microembolism (in CMR)	30 (5.7)	31 (5.9)	61 (11.6)
Asymptomatic contralateral microembolism (in CMR)	12 (2.3)	8 (1.5)	20 (3.8)
Asymptomatic bilateral microembolism (in CMR)	9 (1.7)	14 (2.7)	23 (4.4)
Asymptomatic restenosis	14 (2.3)	10 (1.6)	24 (3.9)
Symptomatic restenosis	0	0	0
Asymptomatic stent 100% occluded	2 (0.3)	1 (0.2)	3 (0.5)
Total	67 (12.3)	64 (12.1)	131 (24.4)

CMR - cranial magnetic resonance

Severe ICA stenosis was detected in 48 (8%) patients before cardiac surgery. To avoid high risk of cardiac surgery, CAS was first performed in these patients. The patients were referred for cardiac surgery 4 weeks after the CAS procedure. In addition to the CAS procedure performed prior to the open heart surgery, a total of 110 (18%) patients were diagnosed with new coronary artery disease via coronary angiography simultaneously performed with the CAS procedure. Percutaneous coronary intervention was performed in 89 (15%) of these patients, while coronary artery bypass surgery was performed in 21 (3.5%) patients 4 weeks after the CAS procedure. Bilateral CAS procedure was performed in 43 (7%) patients. If the patient had no priority in terms of clinic and lesion characteristics, the CAS procedure was first performed on the technically easy side of the ICA. In cases where two carotid lesion stenoses were similar in all aspects, priority was given to the right ICA CAS, which is easier to access. The left ICA CAS procedure was performed 3 weeks later.

CAS was successfully performed with ticagrelor in 56 (9.2%) patients who were found to be resistant to clopidogrel alone. Patients who underwent CAS with ticagrelor had no ischemic or bleeding complications, different from clopidogrel. Forty-three (7%) patients were on warfarin or a new generation oral antico-

agulant for various reasons. In these patients, anticoagulants and dual antiplatelet therapy were continued for 1 month after the CAS procedure. Acetylsalicylic acid was discontinued 1 month later. After 1 year, if the patient did not have a specific need for antiplatelet treatment, clopidogrel was discontinued and anticoagulant therapy alone was maintained (Table 5).

Among patients with a successful CAS, one, 2, and one patient died due to hyperperfusion syndrome, acute carotid artery stent thrombosis, and intracranial bleeding 6 h after the procedure, respectively. Myocardial infarction was not observed in any patient with an electrocardiographic change. Acute carotid artery stent thrombosis was observed in 4 (0.6%) patients. Thrombosis occurred within 4 h after CAS in 3 of the patients and 8 days after CAS in the other patient. Resistance to clopidogrel was detected in early stent thrombosis. The stent thrombosis on the 8th day was due to the discontinuation of clopidogrel by the patient. In 4 patients, no procedure-related complications, coagulopathy-associated syndrome, or mutations that could cause acute carotid artery stent thrombosis were detected.

Two patients experienced hyperperfusion syndrome. One of the patients had a total right ICA occlusion. A total of 99% of stenosis in the left ICA occurred with CAS. The CEA surgery was

Table 5. Special patient groups undergoing CAS

Special group	n (%)
Radiotherapy history and CAS	6 (1)
CAS to CEA restenosis (secondary)	13 (2.1)
CEA/CAS hybrid approach	36 (6)
CAS after acute stroke thrombectomy	13(2)
CAS before cardiac surgery	48 (8)
Bilateral CAS	43 (7)
Clopidogrel resistance and CAS	56 (9.2)
Warfarin/NOAC and CAS	43 (7)

CAS - carotid artery stenting, CEA - carotid endarterectomy, NOAC - new oral anticoagulant

highly risky for the patient. The patient had intracranial hemorrhage after the CAS procedure and later died. The other patient who experienced hyperperfusion improved without sequelae during a medical follow-up with blood pressure regulation.

One (0.2%) patient had gastrointestinal bleeding that did not require transfusion. Acetylsalicylic acid was discontinued at the end of the first month in patients who were followed up with a gastroenterology clinical picture and whose treatment was continued with clopidogrel.

After the procedure, symptomatic sinus bradycardia (41 beats/min), which did not improve with medical treatment, was observed in one patient who had sinus bradycardia (52 beats/min) before CAS. Consequently, a permanent cardiac pacemaker was implanted to the patient. Three (0.5%) patients had acute atrial fibrillation after CAS. However, the patients spontaneously returned to sinus rhythm within 12 h.

Twenty-four (3.9%) cases of restenosis were monitored in a mean 6-year follow-up period. None of the restenosis was symptomatic. CEA surgery was performed to asymptomatic restenosis with an intra-stent restenosis rate of $\geq 80\%$. The stent was surgically removed and endarterectomy was performed in these patients. The stent was 100% occluded in 3 patients 6 months after the CAS procedure (Table 5). Medical follow-up was performed because the patients were asymptomatic. Blood lipid levels, blood sugar, and systemic blood pressure values were closely followed up in patients with restenosis.

Discussion

The success rate of the CAS procedure was found to be 96%. However, death associated with the procedure was observed in 0.6% patients in whom CAS was successfully performed. No patient had myocardial infarction with electrocardiographic changes. In addition, acute carotid artery stent thrombosis was observed in 0.6% patients. Hyperperfusion syndrome was reported in 2 (0.3%) patients. Periprocedural major stroke was observed in 2 (0.3%) patients, whereas periprocedural minor stroke was observed in 12 (1.9%) patients. CDMR showed asymptomatic ipsilateral cranial microembolism, asymptomatic contralateral cranial microembolism, and bilat-

eral asymptomatic cranial microembolism in 61 (11.6%), 20 (3.8%), and 23 (4.4%) patients, respectively. One (0.2%) patient had a persistent bradycardia after the CAS procedure. Three (0.5%) patients had an acute atrial fibrillation after the CAS procedure. Asymptomatic restenosis was observed in 24 (3.9%) patients. In 3 patients, 100% asymptomatic in-stent occlusion was observed 6 months after the CAS procedure.

During medical follow-up, there is a 26% risk of non-revascularized, symptomatic carotid artery stenosis, which causes ischemic stroke within 2 years (4). The annual incidence rate of stroke associated with asymptomatic carotid plaques causing $>60\%$ stenosis during medical follow-up was found to be 2.5% (5). With the development of endovascular treatment methods, CAS has become an alternative treatment option to CEA in the treatment of ICA stenosis (1). The ICA stenosis rate and lesion nature (soft plaques, especially ulcerations) are among the most significant factors in determining the risk of stroke (5). However, studies on carotid artery interventions conducted to date have not yet clearly revealed which treatment method is superior in relation to patient or lesion characteristics.

Several diseases are the area of interest for more than one discipline at the same time. For example, recently, it was emphasized that the decision for percutaneous treatment or open surgery in the treatment of cardiovascular diseases made with the cardiac team will always be more accurate. Interventions for ICA stenosis concern neurology, radiology, cardiology, cardiovascular surgery, and neurosurgery. Literature studies show that the outcomes of CAS procedures performed by specialists with an experience of more than 50 CAS a year were better (3). The success rates of CAS performed by different specialties are also different. The outcomes of CAS procedures performed only by cardiologists or only by interventional neurologists are more successful than the outcomes of CAS procedures performed by other specialties (3). The long-term outcomes of CAS, which were evaluated, implemented, and followed up with a multidisciplinary approach, have not been previously published in the literature.

In our patient series consisting of real-life data, CAS was successfully performed in 610 patients, with lower complication rates as required by the guidelines. We believe that the most significant factor contributing to this result is the multidisciplinary treatment of the carotid artery stenosis. The first factor that would affect CAS results is the symptomatic nature of the ICA stenosis. We believe that this decision should be made especially by a neurologist experienced in dealing with strokes. We consider that the coordination between the neurologist and cardiologist is vital in presenting whether ischemic stroke is caused by the carotid artery stenosis in a symptomatic patient. An essential part of ischemic strokes can be arrhythmic, hemodynamic, and embolism from the prosthetic valve, aortic arch, or patent foramen ovale (6). As with our series, most of the patients with carotid artery stenosis had concomitant coronary artery disease, hypertension, hyperlipidemia, arrhythmia, and heart valve disease. We performed coronary angiography during the same session after the CAS procedure for all patients with no

history of coronary angiography. In the majority of patients, coronary lesions were also detected at the limit where the guidelines recommend indication for coronary revascularization, including the left main coronary artery. If the CAS procedures were performed by a non-cardiologist clinic, coronary artery stenosis, which would have determined survival of the patient, would not have been detected. Hemodynamic follow-up is very significant after the CAS procedure. We followed up our patients who underwent CAS for 24 h in the coronary intensive care unit where hemodynamic follow-up would be effective. Therefore, we believe that the contribution of the cardiologist is central in evaluating both the overall risk of stroke of the patients and the risk of CAS and CEA procedures.

A different aspect of our study is the combined interpretation of carotid Doppler USG and CTA for the evaluation of carotid artery plaque nature and carotid artery anatomy. CTA allows for a clearer evaluation especially in calcified lesions (7). It also allows for a clear evaluation of the aortic arch structure, bulbous level, carotid artery adjacencies, the course of the carotid artery from the aorta to its intracranial branching, and collateral connections. This information is useful in selecting the material to be used in the CAS as well as whether to operate on the carotid artery with CAS or CEA.

Randomized studies of carotid artery stent stenosis in the literature had some limitations. The Carotid and Vertebral Artery Transluminal Angioplasty Study did not use EPM and had low stenting rate (8); the Stent-Protected Angioplasty versus Carotid Endarterectomy study had a very little use of EPM (9); only 39% of experienced specialists in the Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial overshadowed the success of CAS (10). Moreover, a study in the literature compared the 13-year results of CEA and CAS and made conclusions in favor of CEA (11). The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) had been the most successful in terms of patient selection, procedure management, and patient follow-up among the randomized controlled studies performed to date. In the CREST, no significant difference was found between the CAS and CEA groups at the end of 4 years in terms of primary endpoints (death + stroke + myocardial infarction in the first 30 days and stroke on the same side as the intervention) (7.2% and 6.8%) (1). The 10-year results of the CREST were published in 2016. Thus, the primary combined endpoints were 11.8% and 9.9% in the CAS and CEA groups, respectively. No statistically significant difference was observed between the two groups. Major strokes mostly occurred in the early postprocedural period. Ten-year restenosis rates in the CREST were 12.2% and 9.7% in the CAS and CEA groups, respectively (2). None of the previous studies, including CREST, selected the embolism protection device based on the carotid artery anatomy, nature of the carotid lesion, and dominance of the arterial supply to the brain. In our study group, the EPM was used at a very similar rate to the CREST (95%). Although our patients were at a higher risk in terms of lesions and clinical characteristics than the patients in the previous studies, CAS procedures were successfully per-

formed with lower complication and restenosis rates than those reported in the literature.

Common characteristics of patients with periprocedural minor stroke and TIA was the longer duration of the procedure as well as stenoses in the intracranial arteries or vertebral arteries, along with the carotid artery stenosis. As the duration of the procedure increased, the number of ischemic and embolic complications due to catheter manipulations, wire spasms, and proximal blood flow interruptions also increased as expected. We believe that it would be beneficial to perform CAS procedures in these patient groups as fast as possible and keep the peri- and postprocedural systemic blood pressure values higher. The CAS procedure can only be conducted faster in experienced centers.

It was believed that periprocedural silent cranial emboli due to CAS procedure did not constitute a clinical picture during the follow-up. However, in the following years, the silent cranial emboli have been shown to cause dementia, decreased cognitive function (12), and even ischemic stroke (13). We believe that asymptomatic ipsilateral microembolism detected in CDMR may be caused by debris and thrombi separated from carotid artery stenosis during the procedure and contralateral and bilateral microembolisms from catheter manipulations in the aortic arch. If CDMR was not performed after the CAS procedure, these asymptomatic microembolism cases would not be detected. We believe that the determination of arch and carotid artery anatomy with CTA in the multidisciplinary committee before CAS and catheter selection accordingly will reduce the risk of catheter-related complications. In some centers, CAS procedures are performed with non-hydrophilic catheters. We believe that this increases catheter-related complications and prolongs the duration of the procedure. We consider that periprocedural debris or thrombus embolization can be minimized with double protection method in lesions with high lipid or thrombus load.

The late expansion rates of carotid artery stents and higher carotid artery lumen diameter compared with the coronary artery allow for low restenosis rates. Self-expandable stents of the carotid artery reach their widest diameter between 6 months and 1 year (14). The 5-year restenosis rates are very low in procedures performed in keeping with its technique, by selecting the appropriate stent and balloon diameter and not leaving the stent tips on the atheroma plaques (15).

Carotid artery stent was found to be 100% occluded in 3 asymptomatic patients during follow-up. The common characteristic of these 3 patients was that the stent-inserted ICA supplying the brain tissue was supplied by the ipsilateral external carotid artery, vertebral arteries, and contralateral ICA. Carotid artery stenosis rates in all 3 patients were between 80% and 90% in DSA. Unlike sudden acute thrombosis, stent restenosis develops over time. The intracranial collateral circulation of these 3 patients was good. Therefore, these patients remained asymptomatic. CAS was performed without complications in these patients who were followed up with the best medical treatment. However, as to why stents were totally occluded is not well understood.

Another quality of our study that distinguishes it from other studies in the literature is the method of approaching special patient groups. We successfully performed CAS, the revascularization method recommended by the literature, to the carotid artery stenosis of 6 patients who received radiotherapy to the neck area due to laryngeal cancer. Lesions in the carotid arteries exposed to radiotherapy are different from the classical atherosclerotic stenoses. Plaques are in the longer and harder segment. In these patients, predilation with high-pressure (14 atmospheres) was applied to the carotid artery stenosis region with non-compliant balloon, and postdilation was avoided. The high-pressure predilation procedure provided better stent placement on the arterial wall and at the same time eliminated the necessity for a postdilation procedure.

There is limited information in the literature regarding patients with a history of CEA surgery and who developed restenosis. In carotid artery lesions treated with CEA, restenosis may occur either from surgical technique or due to intimal plaque migration from the adjacent carotid tissue (16). This restenotic tissue is harder because it contains more fibrotic tissues than the classical atherosclerotic plaques. We also performed the stenting technique in these lesions after the high-pressure predilation, as with the patients with a history of radiotherapy. We successfully performed the CAS procedure in 13 patients with a history of CEA surgery.

In patients with severe bilateral carotid artery stenosis, CAS may be indicated for carotid artery stenosis on one side and CEA for carotid artery stenosis on the opposite side. In such bilateral stenoses, we performed the CAS procedure first to decrease the risk of developing hemodynamic complications during CEA. One month later, CEA was successfully performed to the other side with carotid artery stenosis without discontinuing the dual antiplatelet treatment.

Another different aspect of our study is its approach to patients with acute ischemic stroke and tandem occlusion (total occlusion of the ICA and middle cerebral artery combined). Endovascular thrombectomy is recommended as a first-class indication in the treatment of acute ischemic stroke (17, 18). For such tandem occlusions, in our clinic, we performed balloon angioplasty using Mo.Ma[®] to the carotid artery during the acute period and then thrombectomy to the intracranial artery. In the treatment of acute stroke, carotid stenting can be delayed if an adequate opening can be achieved with balloon angioplasty in ICA occlusions because the dual antiplatelet treatment that we have to administer after stenting can cause serious intracranial bleeding. We performed the CAS procedure for residual carotid artery stenosis 1 month after the patient's acute period ended and we checked no complications of intracranial bleeding. We continued the dual antiplatelet treatment in this patient group for 1 month.

In patients who were to undergo open cardiac surgery and be connected to the heart-lung machine, concomitant serious lesions in the carotid artery increase the risk of intraoperative stroke (18). Open heart surgery and concomitant CEA increase the duration and risk of surgery (19). In our center, we first per-

formed the CAS procedure to this group of patients, and after the 4-week dual antiplatelet therapy, we performed open heart surgery with lower risk single antiplatelet.

There are two main causes of acute thrombosis after CAS: procedural complications and antiplatelet resistance (20). Among our patients who experienced postprocedural ipsilateral major stroke, the cause of which was acute carotid artery stent thrombosis associated with clopidogrel resistance in 4 patients and plaque prolapse and embolism after balloon postdilation in one patient. Transient episodes of hemiplegia due to a hemodynamic instability were observed in several patients after CAS. The hemodynamic episodes of hemiplegia improved with the infusion of atropine, intravenous saline, and norepinephrine. Balloon postdilation was avoided as much as possible after CAS to prevent plaque prolapse. Routine antiplatelet resistance testing before CAS is not regularly recommended in the guidelines. However, based on our previous experience, the routine antiplatelet resistance is tested in our center before CAS (21, 22). If the patient is resistant to both acetylsalicylic acid and clopidogrel, CEA is preferred. However, if the patient has only resistance to clopidogrel, CAS is performed with ticagrelor instead of clopidogrel (22). We did not observe acute carotid artery stent thrombosis complications in any of our patients after we had started to test the antiplatelet resistance.

Study limitations

Firstly, routine cardiac enzyme was not performed after the CAS procedure. The success and complication rates of our CAS group were not compared with the CEA group. The results of the distal and proximal preservation methods, which are the cranial embolism methods, could not be analyzed. Moreover, the results of the self-expandable stent and technical methods used in the CAS procedure could not be grouped.

Conclusion

We believe that the CAS treatment, including patient groups at risk, is safe with low complication and high success rates in cases which were evaluated, applied, and followed up by a multidisciplinary approach.

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